Please replace the paragraph beginning on page 2, line 24, with the following rewritten paragraph:

A2 In yet another preferred embodiment, an isolated EBI-3-alt nucleic acid molecule has the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a complement thereof.

Please replace the paragraph spanning pages 2-3 with the following rewritten paragraph:

A3 In another embodiment, an isolated nucleic acid molecule of the present invention encodes an EBI-3-alt protein which includes an "N-terminal EBI-3-like domain", and/or a "C-terminal unique domain". In another embodiment, the EBI-3-alt nucleic acid molecule encodes an EBI-3-alt protein and is a naturally occurring nucleotide sequence. In yet another embodiment, an isolated nucleic acid molecule of the present invention encodes an EBI-3-alt protein and comprises a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule complementary to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790.

Please replace the paragraph beginning page 3, line 6 with the following rewritten paragraph:

A4 -- Another embodiment of the invention features EBI-3-alt nucleic acid molecules that specifically detect EBI-3-alt nucleic acid molecules relative to nucleic acid molecules encoding non-EBI-3-alt proteins. For example, in one embodiment, an EBI-3-alt nucleic acid molecule hybridizes under stringent conditions to a nucleic acid which is complementary to a nucleic acid molecule comprising nucleotides 1-868 of SEQ ID NO:1. In another embodiment, the EBI-3-alt nucleic acid molecule is at least 50-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-860, or more nucleotides in length and hybridizes under stringent conditions to a nucleic acid which is complementary to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a complement thereof.

Please replace the paragraph spanning pages 3-4 with the following rewritten paragraph:

--Another embodiment of the invention features an isolated EBI-3-alt protein which is encoded by a nucleic acid molecule having a nucleotide sequence at least about 60% homologous to a nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a complement thereof. This invention also features an isolated EBI-3-alt protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a complement of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a complement thereof. In another embodiment, the polypeptide is fragment of an EBI-3-alt polypeptide comprising the amino acid sequence of SEQ ID NO:2, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, where the fragment comprises at least 5-10 contiguous amino acids of SEQ ID NO:2 (*e.g.*, comprises at least 10 contiguous amino acids of SEQ ID NO:2 from about amino acid 55-192), or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790.

Please replace the paragraph beginning on page 9, line 21 with the following rewritten paragraph:

--A plasmid containing the nucleotide sequence encoding human EBI-3-alt was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, USA, on September 27, 1999 and assigned Accession Number PTA-790. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.

Please replace the paragraph beginning on page 10, line 19, with the following rewritten paragraph:

--A nucleic acid molecule of the present invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a portion thereof,

can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, as a hybridization probe, EBI-3-alt nucleic acid molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A7

Please replace the paragraph beginning on page 10, line 31, with the following rewritten paragraph:

Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790.

A8

Please replace the paragraph beginning on page 11, line 17, with the following rewritten paragraph:

In yet another preferred embodiment, an isolated nucleic acid molecule of the invention comprises the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790. A plasmid containing the full length nucleotide sequence encoding EBI-3-alt was deposited with the American Type Culture Collection (ATCC), Manassas, Virginia, and assigned Accession Number PTA-790.

A9

Please replace the paragraph beginning on page 11, line 22, with the following rewritten paragraph:

-- In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid

A10

deposited with ATCC as Accession Number PTA-790 is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790 such that it can hybridize to a complement of the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, thereby forming a stable duplex.

A10

Please replace the paragraph spanning pages 11-12 with the following rewritten paragraph:

--In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 60-65%, preferably at least about 65-75%, more preferable at least about 75-85%, and even more preferably at least about 85-95%, most preferably 95%-99.9% or more homologous to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a portion of any of these nucleotide sequences. In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9% or more homologous to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3, the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a portion of any of these nucleotide sequences.--

A11

Please replace the paragraph beginning on page 12, line 11, with the following rewritten paragraph:

--Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, for example a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of EBI-3-alt. The nucleotide sequence determined from the cloning of the human EBI-3-alt gene allows for the generation of probes and primers designed for use in identifying and/or cloning EBI-3-alt homologues in other cell types, *e.g.*, from other tissues, as well as EBI-3-alt homologues from other mammals. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that

A12

hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 40, 50 or 75 consecutive nucleotides of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790 sense, or an anti-sense sequence of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or of a naturally occurring mutant of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790.

A12

Please replace the paragraph spanning pages 12-13 with the following rewritten paragraph:

-- A nucleic acid fragment encoding a "biologically active portion of EBI-3-alt" can be prepared by isolating a portion of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790 which encodes a polypeptide having an EBI-3-alt biological activity (the biological activities of the EBI-3-alt proteins have previously been described), expressing the encoded portion of EBI-3-alt protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of EBI-3-alt.

A13

Please replace the paragraph beginning on page 13, lines 6, with the following rewritten paragraph:

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3 and from the nucleotide sequences of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or portions thereof, due to degeneracy of the genetic code and thus encode the same EBI-3-alt protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3 or by the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NO:2.

A14

Please replace the paragraph beginning on page 13, line 27, with the following rewritten paragraph:

Moreover, nucleic acid molecules encoding EBI-3-alt proteins from other species, and thus which have a nucleotide sequence which differs from the human sequences of SEQ ID

A15

NO:1 or SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790 are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the EBI-3-alt cDNA of the invention can be isolated based on their homology to the human EBI-3-alt nucleic acids disclosed herein using the human cDNA, or portions thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions. For example, a viral EBI-3-alt cDNA can be isolated based on its homology to human EBI-3-alt.

Please replace the paragraph spanning pages 13-15 with the following rewritten paragraph:

--Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790. In other embodiment, the nucleic acid is at least 30, 50, 100, 250 or 500 nucleotides in length. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences that are significantly identical or homologous to each other remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85% or 90% identical to each other remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, Ausubel *et al.*, eds., John Wiley & Sons, Inc. (1995), sections 2, 4 and 6. Additional stringent conditions can be found in *Molecular Cloning: A Laboratory Manual*, Sambrook *et al.*, Cold Spring Harbor Press, Cold Spring Harbor, NY (1989), chapters 7, 9 and 11. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 4X sodium chloride/sodium citrate (SSC), at about 65-70°C (or alternatively hybridization in 4X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 1X SSC, at about 65-70°C. A preferred, non-limiting example of highly stringent hybridization conditions are hybridization in 1X SSC, at about 65-70°C (or alternatively hybridization in 1X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 0.3X SSC, at about 65-70 °C. A preferred, non-limiting example of reduced stringency hybridization conditions are hybridization in 4X SSC, at about 50-60°C (or alternatively hybridization in 6X SSC plus 50%

formamide at about 40-45°C) followed by one or more washes in 2X SSC, at about 50-60°C. Ranges intermediate to the above-recited values, *e.g.*, at 65-70 °C or at 42-50°C are also intended to be encompassed by the present invention. SSPE (1xSSPE is 0.15M NaCl, 10mM NaH_2PO_4, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete. The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(°C) = 2(\#\text{ of A + T bases}) + 4(\#\text{ of G + C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(°C) = 81.5 + 16.6(\log_{10}[Na^+]) + 0.41(\%G+C) - (600/N)$, where N is the number of bases in the hybrid, and $[Na^+]$ is the concentration of sodium ions in the hybridization buffer ($[Na^+]$ for 1xSSC = 0.165 M). It will also be recognized by the skilled practitioner that additional reagents may be added to hybridization and/or wash buffers to decrease non-specific hybridization of nucleic acid molecules to membranes, for example, nitrocellulose or nylon membranes, including but not limited to blocking agents (*e.g.*, BSA or salmon or herring sperm carrier DNA), detergents (*e.g.*, SDS), chelating agents (*e.g.*, EDTA), Ficoll, PVP and the like. When using nylon membranes, in particular, an additional preferred, non-limiting example of stringent hybridization conditions is hybridization in 0.25-0.5M NaH_2PO_4, 7% SDS at about 65°C, followed by one or more washes at 0.02M NaH_2PO_4, 1% SDS at 65°C (see *e.g.*, Church and Gilbert (1984) *Proc. Natl. Acad. Sci. USA* 81:1991-1995).

A16

Please replace the paragraph beginning on page 15, line 7, with the following rewritten paragraph:

In addition to naturally-occurring allelic variants of the EBI-3-alt sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, thereby leading to changes in the amino acid sequence of the encoded EBI-3-alt protein, without altering the functional ability of the EBI-3-alt protein. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of EBI-3-alt (*e.g.*, the sequence of SEQ ID NO:2) without altering the

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biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the EBI-3-alt proteins of the present invention, are predicted to be particularly unamenable to alteration. Furthermore, amino acid residues that are conserved between EBI-3-alt proteins and other proteins having N-terminal EBI-3-like domains and/or C-terminal unique domains are not likely to be amenable to alteration.--

A17

Please replace the paragraph beginning on page 16, line 1, with the following rewritten paragraph:

--An isolated nucleic acid molecule encoding an EBI-3-alt protein homologous to the protein of SEQ ID NO:2 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or into the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790 by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in EBI-3-alt is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an EBI-3-alt coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for EBI-3-alt biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with

A18

A18

ATCC as Accession Number PTA-790, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

Please replace the paragraph spanning pages 18-19 with the following rewritten paragraph:

-- In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave EBI-3-alt mRNA transcripts to

A19

thereby inhibit translation of EBI-3-alt mRNA. A ribozyme having specificity for an EBI-3-alt-encoding nucleic acid can be designed based upon the nucleotide sequence of an EBI-3-alt cDNA disclosed herein (*i.e.*, SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an EBI-3-alt-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742. Alternatively, EBI-3-alt mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418. --

Please replace the paragraph spanning pages 35-36 with the following rewritten paragraph:

-- A transgenic animal of the invention can be created by introducing EBI-3-alt-encoding nucleic acid into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The EBI-3-alt cDNA sequence of SEQ ID NO:1 or SEQ ID NO:3, or the DNA insert of the plasmid

A20

deposited with ATCC as Accession Number PTA-790 can be introduced as a transgene into the genome of a non-human animal. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the EBI-3-alt transgene to direct expression of EBI-3-alt protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become

conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Patent No. 4,873,191 by Wagner *et al.* and in Hogan, B., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the EBI-3-alt transgene in its genome and/or expression of EBI-3-alt mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding EBI-3-alt can further be bred to other transgenic animals carrying other transgenes.

Please replace the paragraph spanning pages 52-53 with the following rewritten paragraph:

--An exemplary method for detecting the presence or absence of EBI-3-alt in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting EBI-3-alt protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes EBI-3-alt protein such that the presence of EBI-3-alt is detected in the biological sample. A preferred agent for detecting EBI-3-alt mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to EBI-3-alt mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length EBI-3-alt nucleic acid, such as the nucleic acid of SEQ ID NO:1 or SEQ ID NO:3, the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-790, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to EBI-3-alt mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.--

In the claims:

Please amend claims 1, 2, 8, 9 and 12 as follows:

1. (Amended) An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule comprising a nucleotide sequence which is at least 75% homologous to a nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, the DNA